

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
0609.4350001/REF/KKV

APPLICANT  
BUSH et al.

FILING DATE  
September 8, 1999

GROUP  
To be assigned 1647

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
<del>BOB</del>	AA1	5,242,932	09/07/1993	Gandy et al.	544	313	12/17/1991
	AB1	5,373,021	12/13/1994	Marangos	514	483	04/26/1993
	AC1	5,523,295	06/04/1996	Esamh	514	63	07/06/1994
	AD1	5,688,516	11/18/1997	Raad et al.	424	409	10/03/1994
	AE1	5,688,651	11/18/1997	Solomon	435	7.1	12/16/1994
	AF1	5,705,401	01/06/1998	Masters et al.	436	518	09/16/1994
	AG1	5,707,821	01/13/1998	Rydel et al.	435	18	06/07/1995
<del>BOB</del>	AH1	5,721,106	02/24/1998	Maggio et al.	435	7-8	09/12/1994

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
<del>BOB</del>	AI1	WO 92/18111	10/ 29/1992	WIPO			Yes
<del>BOB</del>	AJ1	WO 93/10439	05/27/1993	WIPO			No
<del>BOB</del>	AK1	WO 93/24451	12/09/1993	WIPO			Yes
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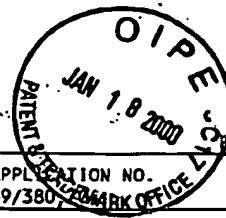
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AL	1	Assaf, S.Y and Chung, S.-H., "Release of endogenous Zn <sup>2+</sup> from brain tissue during activity," Nature 308:734-736 (April 1984).
AM	1	Atwood, C.S. et al., "Dramatic Aggregation of Alzheimer AB by Cu(II) Is Induced by Conditions Representing Physiological Acidosis," J. Biol. Chem. 273:12817-12826 (May 1998).
AN	1	Bacon, P.A. et al., "Rheumatoid Disease, Amyloidosis and its Treatment with Penicillamine," Eur. J. Rheum. Inflamm. 2:70-74 (1979)
AO	1	Barrow, C.J., and Zagorski, M.G., "Solution Structures of $\beta$ Peptide and Its Constituent Fragments: Relation to Amyloid Deposition," Science 253:179-182 (July 1991).
AP	1	Barrow, C.J., et al., "Solution Conformations and Aggregational Properties of Synthetic Amyloid $\beta$ -Peptides of Alzheimer's Disease," J. Mol. Biol. 225:1075-1093 (June 1992).

EXAMINER Bridget P. Dunner

DATE CONSIDERED 9/13/05

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<del>BBB</del>	AI2	WO 94/04167	03/03/1994	WIPO			Yes No
<del>BBB</del>	AJ2	WO 95/34199	11/23/1995	WIPO			Yes No
<del>BBB</del>	AK2	WO 96/07096	03/07/1996	WIPO			Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	2	Basun, H., et al., "Metals and trace elements in plasma and cerebrospinal fluid in normal ageing and Alzheimer's disease," <i>J. Neural Transm. [P-D Sect.]</i> 3:231-258 (1991).
	AM	2	Beht, C., et al., "Hydrogen Peroxide Mediates Amyloid $\beta$ Protein Toxicity," <i>Cell</i> 77:817-827 (June 1994).
	AN	2	Biaglow, J.E. and Kachur, A.V., "The Generation of Hydroxyl Radicals in the Reaction of Molecular Oxygen with Polyphosphate Complexes of Ferrous Ion," <i>Radiation Res.</i> 148:181-187 (August 1997).
	AO	2	Boado, R.J. et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," <i>J. Pharm. Sci.</i> 87(11):1308-1315 (November 1998).
	AP	2	Borman, S., "Diverse Strategies Emerge For Diagnosing Alzheimer's Disease," <i>Chem. Eng. News</i> 272:33-34 (June 1996).

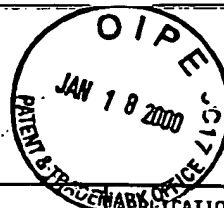
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<del>SOB</del>	A13	WO 96/12544	05/02/1996	WIPO			Yes No
	AJ3	WO 96/28471	09/19/1996	WIPO			Yes No
	AK3	WO 97/04794	02/13/1997	WIPO			Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	3	Bruce, A.J. et al., "β-Amyloid toxicity in organotypic hippocampal cultures: Protection by EUK-8, a synthetic catalytic free radical scavenger," <i>Proc. Natl. Acad. Sci. USA</i> 93:2312-2316 (March 1996).
	AM	3	Burdick, D., et al., "Assembly and Aggregation Properties of Synthetic Alzheimer's A4/β Amyloid Peptide Analogs," <i>J. Biol. Chem.</i> 267:546-554 (January 1992).
	AN	3	Burns, J.A., et al., "Selective Reduction of Disulfides by Tris(2-carboxyethyl)phosphine," <i>J. Org. Chem.</i> 56:2648-2650 (April 1991).
	AO	3	Busciglio, J., and Yankner, B.A., "Apoptosis and increased generation of reactive oxygen species in Down's Syndrome neurons in vitro," <i>Nature</i> 378:776-779 (December 1995).
	AP	3	Bush, A.I., et al., "A Novel Zinc(II) Binding Site Modulates the Function of the βA4 Amyloid Protein Precursor of Alzheimer's Disease," <i>J. Biol. Chem.</i> 268:16109-16112 (August 1993).

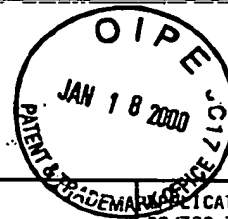
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	A14	WO 97/09976	03/20/1997	WIPO			Yes No
	AJ4	WO 97/36885	10/09/1997	WIPO			Yes No
	AK4	WO 98/06403	02/19/1998	WIPO			Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	4	Bush, A.I., <i>et al.</i> , "Modulation of A $\beta$ Adhesiveness and Secretase Site Cleavage by Zinc," <i>J. Biol. Chem.</i> 269:12152-12158 (April 1994).
	AN	4	Bush, A.I., <i>et al.</i> , "The Amyloid $\beta$ -Protein Precursor and Its Mammalian Homologues," <i>J. Biol. Chem.</i> 269:26618-26621 (October 1994).
	AN	4	Bush, A.I., <i>et al.</i> , "Rapid Induction of Alzheimer A $\beta$ Amyloid Formation by Zinc," <i>Science</i> 265:1464-1467 (September 1994).
	AO	4	Bush, A.I., <i>et al.</i> , Response to "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920-1923 (June 1995).
	AP	4	Butterfield, D.A., <i>et al.</i> , " $\beta$ -Amyloid Peptide Free Radical Fragments Initiate Synaptosomal Lipoperoxidation in a Sequence-Specific Fashion: Implications to Alzheimer's Disease," <i>Biochem. Biophys. Res. Commun.</i> 200:710-715 (April 1994).

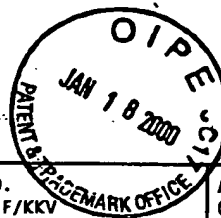
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	AI5	WO 98/40071	09/17/1998	WIPO			Yes No
	AJ5	WO 99/09981	03/04/1999	WIPO			Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	5	Butterfield, D.A., <i>et al.</i> , "A $\beta$ (25-35) Peptide Displays H <sub>2</sub> O <sub>2</sub> -Like Reactivity Towards Aqueous Fe <sup>2+</sup> , Nitroxide Spin Probes, and Synaptosomal Membrane Proteins," <i>Life Sci.</i> 58:217-228 (1996).
	AM	5	Cherny, R.A. <i>et al.</i> , "The Aggregation of A $\beta$ in Human Brain is Mediated by Zinc," <i>Soc. for Neurosci. Abstracts</i> 23:534 (October 1997).
	AN	5	Ohong, Y.-H., and Suh, Y.-H., "Aggregation of amyloid precursor proteins by aluminum in vitro," <i>Brain Research</i> 670:137-141 (January 1995).
	AO	5	Colaco, C.A.L.S., <i>et al.</i> , "The role of the Maillard reaction in other pathologies: Alzheimer's disease," <i>Nephrol. Dial. Transplant.</i> 11(Suppl. 5):7-12 (1996).
	AP	5	Connor, J.R. <i>et al.</i> , "A Histochemical Study of Iron, Transferrin, and Ferritin in Alzheimer's Diseased Brains," <i>J. Neurosci. Res.</i> 31:75-83 (January 1992).

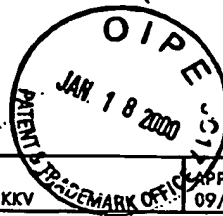
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Dwight E. Bunner

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AL	6	Connor, J.R. et al., "Ceruloplasmin levels in the human superior temporal gyrus in aging and Alzheimer's disease," <i>Neurosci. Lett.</i> 159:88-90 (September 1993).
AM	6	Coyle, J.T., and Puttfarcken, P., "Oxidative Stress, Glutamate, and Neurodegenerative Disorders," <i>Science</i> 262:689-695 (October 1993).
AN	6	Crapper McLachlan, D.R. et al., "Intramuscular desferrioxamine in patients with Alzheimer's disease," <i>Lancet</i> 337:1304-1308 (June 1991).
AD	6	Cuajungco, M.P. and Lees, G.J., "Zinc and Alzheimer's disease: is there a direct link?" <i>Brain Res. Rev.</i> 23:219-236 (April 1997).
AP	6	Dedman, D.J. et al., "Iron and aluminum in relation to brain ferritin in normal individuals and Alzheimer's-disease and chronic renal-dialysis patients," <i>Biochem J.</i> 287:509-514 (1992).

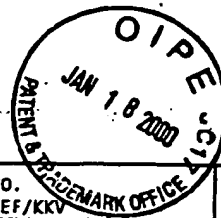
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*Budget E. Bunner*

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## U.S. PATENT DOCUMENTS

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AL	Z	Deibel, M.A. <i>et al.</i> , "Copper, iron, and zinc imbalances in severely degenerated brain regions in Alzheimer's disease: possible relation to oxidative stress," <i>J. Neurol. Sci.</i> 143:137-142 (November 1996).
AM	Z	Doré, S., <i>et al.</i> , "Insulin-like growth factor I protects and rescues hippocampal neurons against $\beta$ -amyloid- and human amylin-induced toxicity," <i>Proc. Natl. Acad. Sci. USA</i> 94:4772-4777 (April 1997).
AN	Z	Dryks, T. <i>et al.</i> , "Amyloidogenicity of $\beta$ A4 and $\beta$ A4-bearing Amyloid Protein Precursor Fragments by Metal-catalyzed Oxidation," <i>J. Biol. Chem.</i> 267:18210-18217 (September 1992).
AO	Z	Ehmann W.D. <i>et al.</i> , "Brain Trace Elements in Alzheimer's Disease," <i>NeuroToxicology</i> 7:197-206 (1986).
AP	Z	Esler, W.P., <i>et al.</i> , "Zinc-Induced Aggregation of Human and Rat $\beta$ -Amyloid Peptides In Vitro," <i>J. Neurochem.</i> 66:723-732 (February 1996).

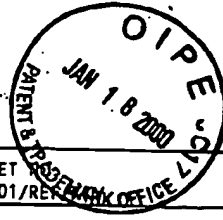
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	AL	8	Esler, W.P., et al., "A $\beta$ deposition inhibitor screen using synthetic amyloid," <i>Nat. Biotechnol.</i> 15:258-263 (March 1997).
	AM	8	Fitzgerald, D.J., "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920 (June 1995).
	AN	8	Folstein, M. "Nutrition and Alzheimer's Disease," <i>Nutrition Reviews</i> 55:23-25 (January 1997).
	AO	8	Fraser, P.E., et al., "pH-dependent structural transitions of Alzheimer amyloid peptides," <i>Biophys. J.</i> 60:1190-1201 (November 1991).
	AP	8	Frederikse, P.H., et al., "Oxidative Stress Increases Production of $\beta$ -Amyloid Precursor Protein and $\beta$ -Amyloid (A $\beta$ ) in Mammalian Lenses, and A $\beta$ Has Toxic Effects on Lens Epithelial Cells," <i>J. Biol. Chem.</i> 271:10169-10174 (April 1996).

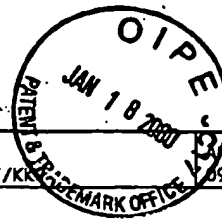
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	AL	2	Frederickson, C.J., "Neurobiology of Zinc and Zinc-Containing Neurons," <i>Int. Rev. Neurobiol.</i> 31:145-238 (1989).				
	AM	2	Frieden, E., "Ceruloplasmin: A Multi-functional Cupro-protein of Vertebrate Plasma," in: <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Clifton, N.J.: Humana Press, pp.159-169 (1982).				
	AN	2	Giampaolo, V., "Copper and Inflammation," in: <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Clifton, N.J.: Humana Press, pp. 329-345 (1982).				
	AO	2	Giulian, D. et al., "Specific Domains of $\beta$ -Amyloid from Alzheimer Plaque Elicit Neuron Killing in Human Microglia," <i>J. Neurosci.</i> 16:6021-6037 (October 1996).				
	AP	2	Glennner, G.G., and Wong, C.W., "Alzheimer's Disease: Initial Report of the Purification and Characterization of Novel Cerebrovascular Amyloid Protein," <i>Biochem. Biophys. Res. Commun.</i> 120: 885-890 (May 1984).				

EXAMINER <i>Bridget E. Bunner</i>	DATE CONSIDERED <i>9/13/05</i>
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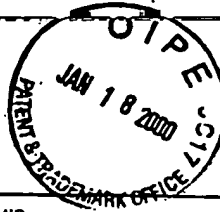
	AL	10	Golde, T.E., et al., "Processing of the Amyloid Protein Precursor to Potentially Amyloidogenic Derivatives," <i>Science</i> 255:728-730 (February 1992).
	AM	10	Good, P.F. et al., "Selective Accumulation of Aluminum and Iron in the Neurofibrillary Tangles of Alzheimer's Disease: A Laser Microprobe (LAMMA) Study," <i>Ann. Neurol.</i> 31:286-292 (March 1992).
	AN	10	Goodman, Y. et al., "Nordihydroguaiaretic acid protects hippocampal neurons against amyloid $\beta$ -peptide toxicity, and attenuates free radical and calcium accumulation," <i>Brain Res.</i> 654:171-176 (August 1994).
	AO	10	Goodman, Y., and Mattson, M.P., "Secreted Forms of $\beta$ -Amyloid Precursor Protein Protect Hippocampal Neurons against Amyloid $\beta$ -Peptide-Induced Oxidative Injury," <i>Exp. Neurol.</i> 128:1-12 (July 1994).
	AP	10	Gorevic, P.D. et al., "The Biological Significance of Amyloid," <i>Ann. New York Acad. Sci.</i> 389:380-394 (1982).

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AL	11	Grundke-Iqbal, I. et al., "Ferritin is a component of the neuritic (senile) plaque in Alzheimer dementia," <i>Acta Neuropathol.</i> 81:105-110 (December 1990).
AM	11	Gutteridge, J.M.C., and Wilkins, S., "Copper Salt-Dependent Hydroxyl Radical Formation Damage to Proteins Acting as Antioxidants," <i>Biochim. Biophys. Acta</i> 759:38-41 (August 1983).
AN	11	Haass, C. et al., "Amyloid $\beta$ -peptide is produced by cultured cells during normal metabolism," <i>Nature</i> 359:322-325 (September 1992).
AO	11	Haley, J.V., "Zinc Sulfate and Wound Healing," <i>J. Surg. Res.</i> 27:168-174 (September 1979).
AP	11	Halliwell, B., and Gutteridge, J.M.C., "Oxygen toxicity, oxygen radicals, transition metals and disease," <i>Biochem. J.</i> 219:1-14 (April 1984).

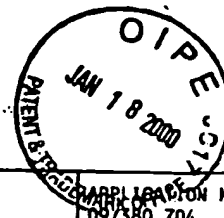
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Bridget E. Dunner

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FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

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## U.S. PATENT DOCUMENTS

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	12	Halliwell, B., "Reactive Oxygen Species and the Central Nervous System," <i>J. Neurochem.</i> 59:1609-1623 (November 1992).
	AM	12	Han, J., <i>et al.</i> , "Quantitation of Hydrogen Peroxide Using Tris(2-carboxyethyl)phosphine," <i>Anal. Biochem.</i> 234:107-109 (February 1996).
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	AO	12	Hansen, M.B., <i>et al.</i> , "Re-examination and further development of a precise and rapid dye method for measuring cell growth/cell kill," <i>J. Immunol. Meth.</i> 119:203-210 (May 1989).
	AP	12	Harman, D., "Aging: A Theory Based on Free Radical and Radiation Chemistry," <i>J. Gerontology</i> 2:298-300 (July 1956).

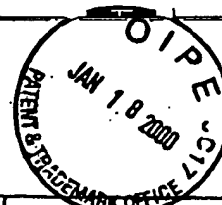
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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AL	13	Harris, M.E., et al., "Direct Evidence of Oxidative Injury Produced by the Alzheimer's $\beta$ -Amyloid Peptide (1-40) in Cultured Hippocampal Neurons," <i>Exp. Neurol.</i> 131:193-202 (February 1995).
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AN	13	Hensley, K et al., "Brain Regional Correspondence Between Alzheimer's Disease Histopathology and Biomarkers of Protein Oxidation," <i>J. of Neurochem.</i> 65:2146-2156 (November 1995).
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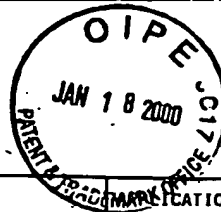
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	AL	14	Hilbich, C., et al., "Aggregation and Secondary Structure of Synthetic Amyloid BA4 Peptides of Alzheimer's Disease," J. Mol. Biol. 218:149-163 (March 1991).
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	AN	14	Hsu, J.M., et al., "Zinc Deficiency and Incorporation of <sup>14</sup> C-labeled Methionine into Tissue Proteins in Rats," J. Nutrition 99:425-432 (December 1969).
	AO	14	Huang, X. et al., "Zinc-induced Alzheimer's Aβ1-40 Aggregation Is Mediated by Conformational Factors," J. Biol. Chem. 272:26464-26470 (October 1997).
	AP	14	Ida, N., et al., "Analysis of Heterogeneous BA4 Peptides in Human Cerebrospinal Fluid and Blood by a Newly Developed Sensitive Western Blot Assay," J. Biol. Chem. 271:22908-22914 (September 1996).

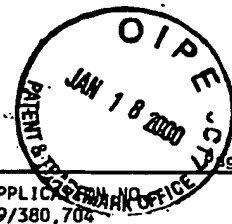
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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL	15	Jarrett, J.T., et al., "The Carboxy Terminus of the $\beta$ Amyloid Protein Is Critical for the Seeding of Amyloid Formations: Implications for the Pathogenesis of Alzheimer's Disease," <i>Biochem.</i> 32:4693-4697 (May 1993).
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	AO	15	Joshi, J.G., "Iron and Aluminum Homeostasis in Neural Disorders," <i>Environ. Health Persp.</i> 102:207-213 (1994).
	AP	15	Kang, J. et al., "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor," <i>Nature</i> 325: 733-736 (February 1987).

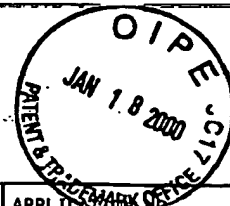
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AL	16	Kawahara, M. et al., "Alzheimer's Disease Amyloid $\beta$ -Protein Forms $Zn^{2+}$ -Sensitive, Cation-Selective Channels Across Excised Membrane Patches from Hypothalamic Neurons," <i>Biophys. J.</i> 73:67-75 (July 1997).
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AO	16	Kirschner, D.A. et al., "Synthetic peptide homologous to $\beta$ protein from Alzheimer disease forms amyloid-like fibrils in vitro," <i>Proc. Natl. Acad. Sci. USA</i> 84:6953-6957 (October 1987).
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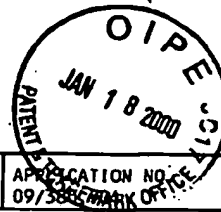
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FORM PTO-1449

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AL	17	Kisilevsky, R., "Inflammation-Associated Amyloidogenesis," <i>Mol. Neurobiol.</i> 8:65-66 (February 1994).
AM	17	Koh, J.Y., and Choi, D.W., "Quantitative determination of glutamate mediated cortical neuronal injury in cell culture by lactate dehydrogenase efflux assay," <i>J. Neurosci. Meth.</i> 20:83-90 (May 1987).
AN	17	Kotaki, H., <i>et al.</i> , "Intestinal Absorption and Metabolism of Clloquinol in the Rat," <i>J. Pharm. Dyn.</i> 6:881-887 (November 1983).
AO	17	Kuo, Y.-M., <i>et al.</i> , "Water-soluble A $\beta$ (N-40, N-42) Oligomers in Normal and Alzheimer Disease Brains," <i>J. Biol. Chem.</i> 271:4077-4081 (February 1996).
AP	17	Landers, J.W., and Zak, B., "Determination of Serum Copper and Iron in a Single Small Sample," <i>Am. J. Clin. Pathol.</i> 29:590-592 (June 1958).

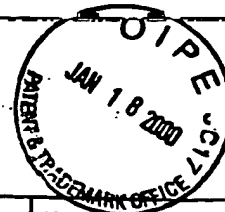
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AL	18	Lindeman, R.D., et al., "Myocardial zinc metabolism in experimental myocardial infarction," J. Lab. Clin. Med. 81:194-204 (February 1973).
AM	18	Lockhart B.P. et al., "Inhibitors of free radical formation fail to attenuate direct beta-amyloid <sub>25-35</sub> peptide-mediated neurotoxicity in rat hippocampal cultures," J. Neurosci. Res. 39:494-505 (November 1994).
AN	18	Lohr, J.B., "Oxygen Radicals and Neuropsychiatric Illness," Arch. Gen. Psychiatry 48:1097-1106 (December 1991).
AO	18	Maggio, J.E., et al., "Zinc and Alzheimer's Disease," Science 268:1920-1921 (June 1995).
AP	18	Mantyh, P.W., et al., "Aluminum, Iron, and Zinc Ions Promote Aggregation of Physiological Concentrations of $\beta$ -Amyloid Peptide," J. Neurochem. 61:1171-1174 (September 1993).

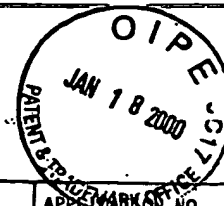
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AL	19	Markesbery, W.R., "Oxidative Stress Hypothesis in Alzheimer's Disease," <i>Free Rad. Biol. Med.</i> 23:134-147 (1997).
AM	19	Masters, C.L., et al., "Amyloid plaque core protein in Alzheimer disease and Down syndrome," <i>Proc. Natl. Acad. Sci. USA</i> 82:4245-4249 (June 1985).
AN	19	Masters, C. L. et al., "Neuronal origin of a cerebral amyloid: neurofibrillary tangles of Alzheimer's disease contain the same protein as the amyloid of plaque cores and blood vessels," <i>EMBO J.</i> 4:2757-2763 (November 1985).
AO	19	Maury, C.P.J., "Biology of Disease: Molecular Pathogenesis of $\beta$ -Amyloidosis in Alzheimer's Disease And Other Cerebral Amyloidoses," <i>Lab. Invest.</i> 72:4-16 (January 1995).
AP	19	McGeer, P.L., and McGeer, E.G., "The inflammatory response system of brain: implications for therapy of Alzheimer and other neurodegenerative diseases," <i>Brain Res. Rev.</i> 21:195-218 (September 1995).

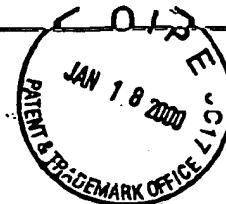
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	AL	20	Mecocci, P., M.D. et al.. "Oxidative Damage to Mitochondrial DNA Shows Marked Age-dependent Increases in Human Brain," <i>Ann. Neurol.</i> 34:609-616 (October 1993).
	AM	20	Menkin, V., "Studies on Inflammation. X. The Cytological Picture of an Inflammatory Exudate in Relation to its Hydrogen Ion Concentration," <i>Am. J. Pathol.</i> 10:193-210 (March 1934).
	AN	20	Michikawa, M., et al.. "Oxygen Radical-Induced Neurotoxicity in Spinal Cord Neuron Cultures," <i>J. Neurosci. Res.</i> 37:62-70 (January 1994).
	AO	20	Milano, R., et al.. "Copper and the Inflammatory Process," <i>Advances in Inflammation Research</i> 1:281-291 (1979).
	AP	20	Moir, R.D. et al.. "Relative Increase in Alzheimer's Disease of Soluble Forms of Cerebral A $\beta$ Amyloid Protein Precursor Containing the Kunitz Protease Inhibitory Domain," <i>J. Biol. Chem.</i> 273:5013-5019 (February 1998).

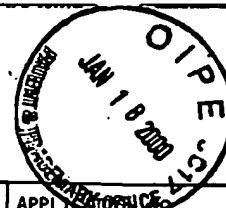
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AL	21	Mok, S.S., et al., "A Novel Metalloprotease in Rat Brain Cleaves the Amyloid Precursor Protein of Alzheimer's Disease Generating Amyloidogenic Fragments," <i>Biochemistry</i> 36:156-163 (January 1997).
AM	21	Multhaup, G., et al., "Interaction between the zinc(II) and the heparin binding site of the Alzheimer's disease BA4 amyloid precursor protein (APP)," <i>FEBS Lett.</i> 355:151-154 (November 1994).
AN	21	Multhaup, G., et al., "The Amyloid Precursor Protein of Alzheimer's Disease in the Reduction of Copper(II) to Copper(I)," <i>Science</i> 271:1406-1409 (March 1996).
AO	21	Munch, G., et al., "Advanced glycation endproducts in ageing and Alzheimer's disease," <i>Brain Res. Rev.</i> 23:134-143 (February 1997).
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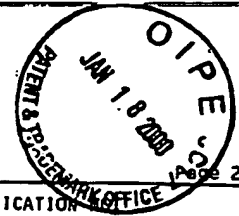
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AL	22	Owen, C.A., Jr., "Uptake of <sup>67</sup> Cu by Ceruloplasmin In Vitro (38878)," <i>Progr. Soc. Exp. Biol. Med.</i> 149:681-682 (July 1975).
AM	22	Padmanabhan, G., et al., "Clioquinol," in: <i>Analytical Profiles of Drug Substances</i> , Volume 18, Florey, K., ed., Academic Press, Inc.: San Diego, CA, pp. 57-90 (1989).
AN	22	Pérez, A.A. et al., "Alzheimer Amyloids Aβ1-40 and Aβ1-42 are Differentially Degraded by Insulin Degrading Enzyme (IDE) From Human Brain," <i>Soc. Neurosci. Abstracts</i> 23:821 (October 1997).
AO	22	Peters, G., and Rodgers, M.A.J., "Single-Electron Transfer from NADH Analogues to Singlet Oxygen," <i>Biochim. Biophys. Acta</i> 637:43-52 (August 1981).
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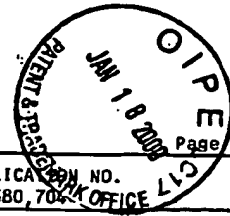
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FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

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## U.S. PATENT DOCUMENTS

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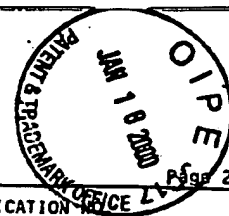
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FORM PTO-1449

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AL	24	Roher, A.E., et al., "Morphology and Toxicity of A $\beta$ -(1-42) Dimer Derived from Neuritic and Vascular Amyloid Deposits of Alzheimer's Disease," <i>J. Biol. Chem.</i> 271:20631-20635 (August 1996).
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AN	24	Sadowski, M. et al., "Astrocyte and microglia reaction in Alzheimer's disease in the hippocampal formation- a quantitative analysis," <i>Alzheimer's Res.</i> 1:71-76 (1995).
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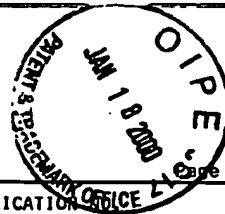
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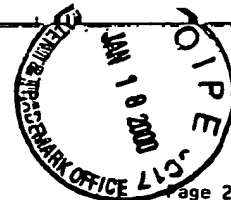
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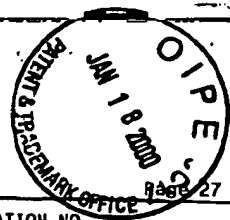
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AL	27	Smith, C. et al., "The molecular pathology of Alzheimer's disease: are we any closer to understanding the neurodegenerative process?," <i>Neuropathol. Appl. Neurobiol.</i> 20:322-38 (August 1994).
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AL	28	Soto, C., et al., "Structural Determinants of the Alzheimer's Amyloid $\beta$ -Peptide," <i>J. Neurochem.</i> 63:1191-1198 (October 1994).
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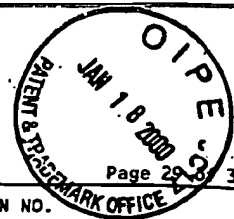
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AL	29	Tateishi, J. et al., "Strain-differences in dogs for neurotoxicity of clioquinol," <i>Lancet</i> 1:1289-1290 (June 1972).
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AP	29	Tateishi, J. et al., "Neurotoxicity of Clioquinol. Part III: Autoradiographic Distribution of Radioactive Clioquinol in Several Species of Animals," <i>Psychiat. Neurol. Jap.</i> 75:187-196 (1973).

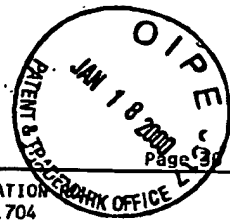
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	AL	30	Tateishi, J. et al., "Neurotoxicity of Clloquinol in Laboratory Animals," <i>Lancet</i> 2:1095 (November 1972).
	AM	30	Teller, J.K., et al., "Presence of soluble amyloid $\beta$ -peptide precedes amyloid plaque formation in Down's Syndrome," <i>Nature Med.</i> 2:93-95 (January 1996).
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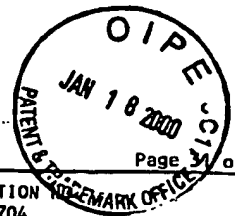
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	AL	31	Tomiyama, T., et al., "Inhibition of Amyloid $\beta$ Protein Aggregation and Neurotoxicity by Rifampicin," <i>J. Biol. Chem.</i> 271:6839-6844 (March 1996).
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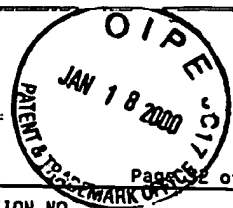
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	AN	32	Wood, S.J., <i>et al.</i> , "Physical, Morphological and Functional Differences between pH 5.8 and 7.4 Aggregates of the Alzheimer's Amyloid Peptide A $\beta$ ," <i>J. Mol. Biol.</i> 256:870-877 (March 1996).
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	AP	32	Zagorski, M.G., and Barrow, C.J., "NMR Studies of Amyloid $\beta$ -Peptides: Proton Assignments, Secondary Structure, and Mechanism of an $\alpha$ -Helix $\rightarrow$ $\beta$ -Sheet Conversion for a Homologous, 28-Residue, N-Terminal Fragment," <i>Biochemistry</i> 31:5621-5631 (June 1992).

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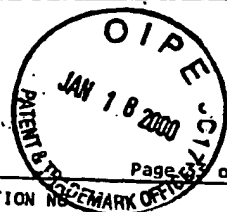
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Dudget E. Bunner

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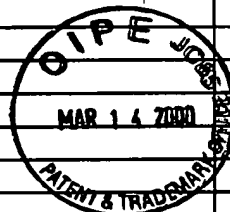
9/13/05

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449 <b>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</b>	ATTY. DOCKET NO. 0609.4350001/REF/KKV	APPLICATION NO. 09/380,704
	APPLICANT BUSH et al.	
	FILING DATE September 8, 1999	GROUP To be assigned <u>147</u>

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA2	5,337,636	10/25/1994	Bresdner, Jr. et al.	2	161.7	06/30/1992
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						



## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL			
	AM			
	AN			
	AO			
	AP	33	Nakada, I. and I.-L. Kwee, "Guanidinoethane sulfate: brain pH alkaline shifter," <i>NeuroReport</i> 4:1035-1038 (August 1993)	

EXAMINER

*Bridget E. Dunner*

DATE CONSIDERED

9/13/05

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FORM PTO-1449  <b>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</b>				ATTY. DOCKET NO. 0609.4350001/REF/KKV		APPLICATION NO. 09/380,704	
APPLICANT BUSH et al.				FILING DATE September 8, 1999		GROUP To be assigned 1647	

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						

FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AL	34	<del>Schrader-Fischer, G. and P.A. Paganetti, "Effect of alkalizing agents on the processing of the <math>\beta</math>-amyloid precursor protein," <i>Brain Research</i> 716:91-100 (April 1996)</del>
	AM		
	AN		
	AO		
	AP		

EXAMINER <i>Bridget E. Bunner</i>	DATE CONSIDERED 9/13/05
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